

AMENDMENTS

Amendments to the claims

Please amend the currently pending claim set as follows:

1-74. (cancelled)

75. (currently amended) A method of determining the genotype of a subject at a locus within genetic material obtained from a biological sample from the subject, the method comprising:

A-(A) reacting the material from said biological sample at the locus to produce a first reaction value indicative of the presence of a given first allele at the locus within said genetic material, wherein the first reaction value is a measure of the intensity of an a first allele-specific quantitative signal;

~~B—forming a data set including the first reaction value;~~ (B) reacting the material from said biological sample at the locus to produce a second reaction value indicative of the presence of a second allele at the locus within said genetic material, wherein the second reaction value is a measure of the intensity of a second allele-specific quantitative signal;

~~G—~~ (C) calculating a set of probability distributions from a set of input data, wherein said set of input data is obtained under conditions that are comparable to the conditions under which the first reaction value and the second reaction value are obtained, wherein said set of probability distributions comprises establishing a distribution-set of probability-distributions, including at least one probability distribution, associating that associates a hypothetical first

reaction value and a hypothetical second reaction value

intensities with a corresponding probabilities for each a genotype of interest

at the locus;

~~D~~(D) applying the first reaction value of step (A) and the second reaction value
of step (B) to each pertinent probability distribution for each genotype of interest
within said set of probability distributions of step (C) to determine a measure of a
the conditional probability of each genotype of interest at the locus, wherein the
conditional probability is a measure of the likelihood of the genotype of interest at
the locus given the first reaction value of step (A) and the second reaction value
of step (B); and

(E) determining the genotype of said subject at the locus based on the measure of
conditional probability of step (D) of each genotype of interest at the locus for
said subject data obtained from step (D), wherein each allele is a single specific
nucleotide.

76. (currently amended) A method according to claim 75, wherein the ~~distribution set of~~
probability distributions of step (C) includes a plurality of probability
distributions for a corresponding plurality of genotypes of interest.

77 -84 (cancelled)

85. (currently amended) A method according to claim 75, wherein step (E) further includes ~~a~~ the step of calculating a confidence score, associated with the determination of the genotype in step (E), based on the measure of conditional probability data from step (D).

86. (currently amended) A method according to claim ~~80~~ 75, wherein step (E) further includes ~~a~~ the step of calculating a confidence score, associated with the determination of the genotype in step (E), based on the measure of conditional probability data from step (D), and the method further comprising:

(~~F~~) determining whether a significant downward trend in confidence scores has occurred, and, in such event, entering an alarm condition.

87-93. (cancelled)

94. (currently amended) A method according to claim 75, wherein step (A) and step (B) each include a ~~(A) includes the~~ step of assaying for the given allele using genetic bit analysis, allele-specific hybridization, or allele-specific amplification, including such amplification by a polymerase chain reaction or a ligase chain reaction.

95-116. (canceled).

117. (currently amended) ~~The A method according to of claim 146~~ 75, wherein step (A) A includes the step of hybridizing a first oligonucleotide probe to the genetic material at the locus and step (B) B includes the step of hybridizing a second oligonucleotide probe to the genetic material at the locus, wherein the first oligonucleotide probe and the second oligonucleotide probe ~~probes~~ are specific for the first allele and the second allele ~~alleles~~, respectively, at the locus.

118. (canceled)

119. (new) A method according to claim 75, wherein step (A) is performed before step (C).

120. (new) A method according to claim 75, wherein step (C) is performed before step (A).

121. (new) A method according to claim 75, wherein the first allele-specific quantitative signal and the second allele-specific quantitative signal are each an optical signal.

122. (new) A method according to claim 75, wherein the set of input data of step (C) includes the first reaction value and the second reaction value.

123. (new) A method for determining a genotype of a subject at a locus within genetic material obtained from a biological sample from said subject, the method comprising:

- (A) reacting the material from said biological sample at the locus to produce a first reaction value indicative of the presence of a first allele at the locus within said genetic material, wherein the first reaction value is a measure of the intensity of a first allele-specific quantitative signal;
- (B) reacting the material from said biological sample at the locus to produce a second reaction value indicative of the presence of a second allele at the locus within said genetic material, wherein the second reaction value is a measure of the intensity of a second allele-specific quantitative signal;
- (C) accessing a set of input data, wherein said set of input data is comprised of pairs of data that are obtained under conditions that are comparable to the conditions under which said first reaction value and said second reaction value are obtained;
- (D) accessing an initial set of probability distributions, wherein said initial set of probability distributions comprises at least one probability distribution that associates a pair of hypothetical reaction values comprised of a first hypothetical reaction value and a second hypothetical reaction value with a corresponding probability for a genotype of interest at the locus;
- (E) applying the input data of step (C) to said initial set of probability distributions of step (D) to obtain a set of initial conditional probabilities of genotypes given the set of input data of (C);

(F) forming a second set of probability distributions by applying data comprising the set of input data of step (C) and the initial conditional probabilities of genotypes of step (E), wherein said second set of probability distributions comprises at least one probability distribution that associates hypothetical pairs of reaction values with corresponding probabilities for a genotype of interest at the locus; and

(G) applying said first reaction value and said second reaction value to the second set of probability distributions of step (F) to determine a measure of a conditional probability of each genotype of interest at the locus, wherein the conditional probability is a measure of the likelihood of the genotype of interest of the subject at the locus given the first reaction value and the second reaction value; and

(H) determining the genotype of said subject at the locus based on the measure of conditional probability of step (G) of each genotype of interest at the locus for said subject, wherein each allele is a single specific nucleotide.

124. (new) A method according to claim 123, wherein said second set of probability distributions is calculated to maximize the total likelihood of genotypes given the set of input data.

125. (new) A method according to claim 123, wherein each pair of data in the set of input data of step (C) is expressed as a single numerical value.

126. (new) A method according to claim 125, wherein the single numerical value is a ratio of the first reaction value and the second reaction value.
127. (new) A method according to claim 123, wherein step (H) further includes a step of calculating a confidence score associated with the determination of the genotype in step (H), based on the measure of conditional probability from step (G).
128. (new) A method according to claim 123, wherein step (F) further includes a step of calculating assumed genotypes for the set of input data of step (C) based on the initial conditional probabilities of genotypes of step (E), wherein the second set of probability distributions is formed by applying data comprising the set of input data of step (C) and the assumed genotypes for the set of input data.
129. (new) A method according to claim 123, wherein the set of input data of step (C) includes the first reaction value and the second reaction value.
130. (new) A method according to claim 123, wherein the first allele-specific quantitative signal and the second allele-specific quantitative signal are each an optical signal.
131. (new) A method for determining a genotype of a subject at a locus comprising the method of claim 123, wherein step (A) is performed before step (C).

132. (new) A method for determining a genotype of a subject at a locus comprising the method of claim 123, wherein step (C) is performed before step (A).
133. (new) A method for determining a genotype of a subject at a locus within genetic material obtained from a biological sample from said subject, the method comprising:
- (A) reacting the material from said biological sample at the locus to produce a first reaction value indicative of the presence of a first allele at the locus within said genetic material, wherein the first reaction value is a measure of the intensity of a first allele-specific quantitative signal;
 - (B) reacting the material from said biological sample at the locus to produce a second reaction value indicative of the presence of a second allele at the locus within said genetic material, wherein the second reaction value is a measure of the intensity of a second allele-specific quantitative signal;
 - (C) accessing a set of input data, wherein said set of input data is comprised of pairs of data that are obtained under conditions that are comparable to the conditions under which said first reaction value and said second reaction value are obtained;
 - (D) making a genotype guess for pairs of data in the set of input data;
 - (E) calculating a set of probability distributions from the pairs of data in the set of input data and from the genotype guesses associated with the pairs of data, wherein said set of probability distributions comprises at least one probability

distribution that associates a hypothetical first reaction value and a hypothetical second reaction value with a corresponding probability for a genotype of interest at the locus;

(F) applying said first reaction value and said second reaction value to each probability distribution of interest of step (E) to determine a measure of a conditional probability of each genotype of interest at the locus, wherein the conditional probability is a measure of the likelihood of the genotype of interest of the subject at the locus given the first reaction value and the second reaction value; and

(G) determining the genotype of the subject at the locus based on the measure of conditional probability of step (F), wherein each allele is a single specific nucleotide.

134. (new) A method according to claim 133, wherein the set of input data includes the first reaction value and the second reaction value.

135. (new) A method according to claim 133, further comprising a step of modifying the set of probability distributions of step (E) to find the maximally likely set of genotype assignments given the set of input data.

136. (new) A method according to claim 133, wherein the genotype guess of step (D) is made from a heuristic algorithm.

137. (new) A method according to claim 133, wherein the pairs of data of step (D) are a subset of the set of input data.
138. (new) A method for determining a genotype of a subject comprising the method of claim 133, wherein step (A) is performed before step (C).
139. (new) A method for determining a genotype of a subject comprising the method of claim 133, wherein step (C) is performed before step (A).